POC Tests for STIs: Can we Point to Over the Counter (OTC)

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FDA
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Disclosures

• I have received funding for research grants and/or have been a lecturer for Becton Dickinson, Gen-Probe Hologic, Abbott Molecular, Siemens Health Care Diagnostics, Cepheid, and Quidel
Background: U.S. Estimates

Estimated Prevalence of Sexually Transmitted Infections in the U.S.
(Total 110,197,000)

Estimated New Sexually Transmitted Infections in the U.S.
(Total 19,738,800/Year)

Objectives

1. To review clinicians and patient needs for POC STIs tests
2. To discuss current and update new POC tests in the pipeline
3. To demonstrate use of STI testing via the Internet for Home Collection/Test
4. To ascertain possibility of pointing to OTC
5. To mention impact of POC testing-advantages and barriers
Introduction: NIH POC for STDs

1. Testing Core

- Survey and testing of new/existing POC tests
- Acceptability of self-collection of STD samples via Internet recruitment
- Self testing for HIV in the JHU ED
- Self testing for Trichomonas POC
- Dev. New POC: MAMEF POC/CT (UMBC)
Introduction: NIH POC for STDs

2. Development Core
   • Solicitation for new CT-POC
   • Walex Evaluations (Applied Physics Lab)
   • FDA- Readiness Consultant

3. Needs Assessment Core
   • Focus Groups, Surveys, Questionnaires

4. Training Core
   • Training of commercial POC developers

5. Administrative Core
   • Admin Manager, Statistics Manager
   • Financial Manager, Cost-Effectiveness
Program Pipeline

Core 1
IN HOUSE CLINICAL TESTING OF PROTOTYPE DEVICES

Core 2
Plan for identifying Collaborative Exploratory Projects
Generate RFP Select Provide Grants to: Researchers Companies

Core 3
NEEDS ASSESSMENT & DISSEMINATION
Clinicians Patients

Core 4
TRAINING & EDUCATION
Biochemists Engineers Administrators

Core 5
ADMINISTRATION

Admin & management services, facilitation, record keeping, operations

FDA Cleared for 1st Care/OTC

NEW TECHNOLOGY

GATHER INFORMATION & DISSEMINATE VIA

Future

Future Impact

Pilot Test 1st Care

1st Clinician Testing

2nd Clinician & Patient testing

Possible OTC Testing
Overview: Laboratory and Point-of-Care Tests for STIs

**Chlamydia trachomatis (CT)**

**Neisseria gonorrhoeae (NG)**

**Trichomonas vaginalis (TV)**

**Syphilis**

**Herpes Simples Virus (HSV)**

**HIV**

Gaydos, C. Rapid Tests for STDs Current Infect Dis Reports 2006;8:115-124

Huppert et al. Point of Care tests for STIs: What’s the Point? Point of Care Journal, 2009

What Are Current POCs?

- **CT** - Clearview (Inverness);
  Cx 49.7% sens; vag 32.8% sens
- **NG** - None FDA cleared but Gram Stain
- **Trichomonas** - Wet preparation - OSOM
- **Syphilis** - RPR, VDRL; sensitive, not specific; FS POC
- **HSV** - Tzanck Smear; IsoAmp® HSV Assay
- **HIV** - Oral fluid antibody tests; Many other FS POCs

New POC tests for STIs

- Chlamydia
- Gonorrhea
- Trichomonas
- Syphilis
- HSV
- HIV
Use of POC in Clinical Settings

• Immediate treatment before patient leaves the clinic; no loss to follow-up

• Impact on disease epidemic?
  – Decrease interval of disease spread

• Impact on behavior?
  – Counseling on risk reduction

• ASSURED Criteria
  – When is a test good enough?
Needs Assessment of Clinicians: Build Your Own Test

• For which organisms do Clinicians want a POC test? (Most say chlamydia)
• How sensitive? (most important -90-99%)
• How specific? (99%)
• How fast does it have to be? (-20 min)
• What about cost? (second most important- $20)
• What about equipment? (no or little equipment)

Forced Choice Questions used in a survey with multivariate analysis

What about Patients Needs?

- Willingness to wait is important
- Willingness to self-collect specimens is important
- Willingness to pay is important
Patient Focus Group and Clinic Questionnaire about POC Tests (N = 371)

<table>
<thead>
<tr>
<th>Specimen Type Preference</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>15.4%</td>
</tr>
<tr>
<td>Vaginal</td>
<td>50.9%</td>
</tr>
<tr>
<td>Urine</td>
<td>33.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Willingness to Wait</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 min</td>
<td>59.0%</td>
</tr>
<tr>
<td>40 min</td>
<td>20.8%</td>
</tr>
<tr>
<td>60 min</td>
<td>10.8%</td>
</tr>
<tr>
<td>90 min</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Willingness to Pay</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10</td>
<td>46.6%</td>
</tr>
<tr>
<td>$20</td>
<td>31.0%</td>
</tr>
<tr>
<td>$30</td>
<td>10.8%</td>
</tr>
<tr>
<td>$40</td>
<td>2.7%</td>
</tr>
<tr>
<td>$50</td>
<td>8.9%</td>
</tr>
</tbody>
</table>

Self-collected vaginal swabs:
- Easy: 80.9%
- Hard: 16.1%
- OK: 3.0%

Barnes et al. 2014 CDC STD Conf, Atlanta GA
POC tests for STIs: What do “end users” want? (N=58, 5 focus groups)

- Favorable POCTs (Rapid, Easy to read, Simple to use)
- Home testing acceptable – better privacy
- Clinic-based- definitive results & immediate treatment
- Barriers- cost and ability to read and perform tests
- Hispanic patients questioned home test reliability, wanted bi-lingual instructions

Table 1. Advantages of having access to a STI point-of-care test in the clinic or at home

<table>
<thead>
<tr>
<th>Settings</th>
<th>Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the clinic</td>
<td>Know the results right away</td>
</tr>
<tr>
<td></td>
<td>Saves time</td>
</tr>
<tr>
<td></td>
<td>Quicker services</td>
</tr>
<tr>
<td></td>
<td>Do not have to wait</td>
</tr>
<tr>
<td>At home</td>
<td>Convenience-</td>
</tr>
<tr>
<td></td>
<td>Confidentiality</td>
</tr>
<tr>
<td></td>
<td>Confidentiality</td>
</tr>
<tr>
<td></td>
<td>Privacy</td>
</tr>
<tr>
<td></td>
<td>No appointment needed</td>
</tr>
<tr>
<td></td>
<td>No need to go to clinic</td>
</tr>
<tr>
<td></td>
<td>Less embarrassment</td>
</tr>
<tr>
<td></td>
<td>Increased health awareness</td>
</tr>
<tr>
<td></td>
<td>Empowerment</td>
</tr>
</tbody>
</table>

Rompalo et al. Sexual Health 2013;10:541-545
Chlamydia trachomatis and Neisseria gonorrhoeae
Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* — 2014

- Nucleic acid amplification tests (NAATS) are recommended for genital infections
  - Vaginal swabs for women
  - Urine for men and women
  - Endocervical swabs
- NAATs are recommended for rectal and oropharyngeal infections (no FDA cleared assay)
- Culture is still required
  - *N. gonorrhoeae* culture capacity is still needed for evaluating suspected cases of treatment failure and monitoring antimicrobial susceptibility

“Near Patient” Test for Chlamydia and Gonorrhea

GeneXpert® CT/NG, Cepheid (90 minutes)

Urine or female Swab samples in Transport Reagent

Transfer the sample to the cartridge

Insert cartridge and start assay

Total hands-on time: <1 Minute

### Results CT/NG

1,722 female & 1,387 males

#### Xpert CT/NG vs. Patient Infected Status

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT Cervical</td>
<td>97.4%</td>
<td>99.6%</td>
</tr>
<tr>
<td>CT Vaginal</td>
<td>98.7%</td>
<td>99.4%</td>
</tr>
<tr>
<td>CT Female Urine</td>
<td>97.6%</td>
<td>99.8%</td>
</tr>
<tr>
<td>NG Cervical</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>NG Vaginal</td>
<td>100%</td>
<td>99.9%</td>
</tr>
<tr>
<td>NG Female Urine</td>
<td>95.6%</td>
<td>99.9%</td>
</tr>
<tr>
<td>CT Male Urine</td>
<td>97.5%</td>
<td>99.9%</td>
</tr>
<tr>
<td>NG Male Urine</td>
<td>98.9%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

What about new CT/NG tests coming along?

1. MAMEF-based DNA detection (microwave accelerated metal enhanced fluorescence)
2. Atlas Velox TM System
3. LAMP Assay
4. MobiLab
1. MAMEEF-based DNA detection

- Microwave-based lysing
- Ultra-rapid and sensitive detection of biomolecules

Microwave-Accelerated Metal-Enhanced Fluorescence DNA detection

- Fluorescent Probe: 22 nt
- Target Sequence: 47 nt
- Anchor Probe: 21 nt
Clinical evaluation of CT MAMEF

![JCM logo](JCM.png)

JCM 2013;51:2913-2920

**Blind Evaluation of the Microwave-Accelerated Metal-Enhanced Fluorescence Ultrarapid and Sensitive Chlamydia trachomatis Test by Use of Clinical Samples**

Johan H. Melendez, Jill S. Huppert, Mary Jett-Goheen, Elizabeth A. Hesse, Nicole Quinn, Charlotte A. Gaydos, Chris D. Geddes

Institute of Fluorescence and Department of Chemistry and Biochemistry, University of Maryland Baltimore County, Baltimore, Maryland, USA; Cincinnati Children's Hospital Medical Center, Division of Gynecology, Cincinnati, Ohio, USA; Division of Infectious Diseases, Johns Hopkins University Medical School, Baltimore, Maryland, USA.

- 257 vaginal swabs – 245 adolescents and young women

<table>
<thead>
<tr>
<th></th>
<th>NAAT+ / MAMEF</th>
<th>NAAT+ / MAMEF</th>
<th>NAAT-/ MAMEF</th>
<th>NAAT-/ MAMEF</th>
<th>Clinical Sensitivity (%)</th>
<th>Concordance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptic plasmid</td>
<td>37</td>
<td>8</td>
<td>15</td>
<td>197</td>
<td>82.2</td>
<td>91.1</td>
</tr>
<tr>
<td>16S rRNA</td>
<td>34</td>
<td>11</td>
<td>15</td>
<td>197</td>
<td>75.5</td>
<td>89.9</td>
</tr>
<tr>
<td>Both assays</td>
<td>33</td>
<td>12</td>
<td>15</td>
<td>197</td>
<td>77.3</td>
<td>89.5</td>
</tr>
</tbody>
</table>

-Less than 10 minutes       $1.50 per test       $2,500 reader
Microwave Irradiation on *Neisseria gonorrhoeae*

- Testing of 20 dry vaginal swabs by MAMEF
- Rapid lysis of cells, fragmentation, and detection of target DNA can be carried out in <10 minutes.
- Detection of GC target DNA is mediated by a fluorescent probe-based approach

<table>
<thead>
<tr>
<th>MAMEF</th>
<th>NAAT</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>1</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

1 – DNA ladder
2 – Unlysed GC cells
3 – Lysed GC – lysing chamber
4 – Lysed GC – microfluidic lysing

Melendez J et al. ASM poster Sunday 10:45 AM - 12:00 PM, Poster Board #133
2. Atlas Velox TM System

- Small footprint platform
- Low cost, No reagents on board
- No fragile optical sensors
- Portable – Robust reader for POC settings

Disposable cartridge
- Reagent stabilised on card
- 20 minutes
- Simple to use system - designed to meet CLIA Waiver
  - Chlamydia (lead product)
  - Chlamydia & Gonorrhea

- Electrochemical label released from probe hybridised by nuclease enzyme


Adlerstein D et al 29th IUSTI European conf on Sex Transmit Dis. Stiges Barcelona Sept 2015
100 patient samples determined to be positive or negative for Chlamydia using the BD test

<table>
<thead>
<tr>
<th></th>
<th>Disease Present</th>
<th>Disease Absent</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>49</td>
<td>0</td>
<td>49</td>
</tr>
<tr>
<td>negative</td>
<td>1</td>
<td>50</td>
<td>51</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>50</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

98% sensitivity
100% specificity

306 patient samples determined to be positive or negative for Chlamydia using Roche or Gen-Probe test

<table>
<thead>
<tr>
<th>Johns Hopkins Results</th>
<th>GeneProbe/Roche Assay Result</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atlas Genetics Assay Result</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>105</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>2</td>
<td>195</td>
<td></td>
</tr>
</tbody>
</table>

98% sensitivity
98% specificity

Atlas Genetics io™ System

The io™ Cartridge

- All reagents required to perform the test are present on the Cartridge
- Ambient storage with >12 month shelf-life
- Multiple tests can be performed on a single Cartridge at the same time
- Broad range of clinical sample types
- Simple disposable provided to add sample to Cartridge
- Volume manufacturing established at Consort Medical plc
Atlas Genetics io™ System

The io™ Reader

- Low cost instrument
- Simple to use
- Small footprint
- No on-board reagents
- Robust. No fragile optical sensors
- Minimal calibration and servicing required
- Results provided as clear, unambiguous output. No interpretation or analysis needed
The Public Health England user trial has tested 186 swab samples

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Atlas Correct</th>
<th>Clinical Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>Confirmed</em> Positive samples</em>*</td>
<td>18</td>
<td>17</td>
<td>94.4%</td>
</tr>
<tr>
<td><em><em>Confirmed</em> Negative Samples</em>*</td>
<td>168</td>
<td>163</td>
<td>97.0%</td>
</tr>
</tbody>
</table>

*Confirmed sample status established from GenProbe Aptima 2 test*
3. LAMP At Point of Use

- Single use, totally disposable
- Fully self contained / Self-powered
- Uses proprietary isothermal amplification
- No training needed
- Highly accurate\(^1\)
- Fast swab to result in 20 minutes
- Highly economical

\(^1\) 98% specificity 99% sensitivity

Mahony et al.
4. MobiLab: A low-cost mobile NAAT platform for Chlamydia

- A Smartphone-enabled microfluidic NAAT
- Three units: a droplet pendant microfluidic cartridge, a battery-powered instrument for droplet manipulation and amplification, and a smartphone for user interface, data acquisition and processing
- A single-stream loop-mediated isothermal amplification (LAMP) assay
- Magnetic particles capture nucleic acid targets from sample lysate via electrostatic interaction.
Chlamydia detection with droplet platform

Droplet cartridge platform

C. Chiou and D. J. Shin et al., Biosens Bioelectron, 2013
Results For the base-case scenario (POC sensitivity 92.9%; 47.5% of women willing to wait 40 min for test results; test cost $33.48), POC was estimated to save US$5050 for each case of PID averted compared with NAAT.

One-way sensitivity analyses indicated that POC would dominate NAAT if the POC test cost is <US$41.52 or if POC sensitivity is ≥87.1%. In a probabilistic sensitivity analysis (Monte Carlo simulations, 10,000 iterations), 10.8% of iterations indicated that the POC strategy dominated the NAAT strategy.

The mean incremental cost-effectiveness ratio indicated that the POC strategy would save US$28 in total, and avert 14 PID cases.
Trichomonas vaginalis

- Wet Preparation - 55%–65% sensitive
- Affirm - 46.3% sensitive
- OSOM POC - 83.3-90% sensitive

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet prep</td>
<td>55%–65%</td>
<td>100%</td>
</tr>
<tr>
<td>Culture</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>POCT (OSOM)</td>
<td>&gt;83%</td>
<td>&gt;97%</td>
</tr>
<tr>
<td>PCR (LDT)</td>
<td>83-92%</td>
<td>100%</td>
</tr>
<tr>
<td>TMA AptimaTV</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>ProbTec TVQ</td>
<td>98.3%</td>
<td>98.3%</td>
</tr>
</tbody>
</table>

Van Der Pol; Schwebke; Taylor: Posters STI & AIDS, 2013.
OSOM Rapid TV Antigen Test

- Immunochromatographic detection
- TV membrane proteins
- Mouse antibodies
- Latex beads/capillary action

Huppert et al, JCM 2005; STI 2007: Sensitivity 83-90%, Specificity 98-100%

Positive:
- A blue Test Line and a red Control Line is a positive result.

Negative:
- A red Control Line but no blue Test Line is a negative result.
Rapid Trichomonas Test as a Model for Better STI Detection

- Trichomonas is an important pathogen
- An accurate rapid test is available
- Evaluate the rapid test as a non-invasive test in adolescents
- Opportunity to explore the impact of rapid testing on acceptability
- Apply this knowledge to other STIs as tests become available
Acceptability of Self-testing for Trichomoniasis

- 15-item Survey: rated on a 3 point Likert scale, “not at all” “somewhat” “very”

- Four subscales:
  - comfort in collecting a self-swab
  - trust in test result
  - self-efficacy
  - confidence in ability to self-swab and perform the test.

- Compared
  - Self- to clinician- testing at baseline
  - Self-testing over time
  - Self-trust to clinician- testing over time

Huppert et al. STI, 2010, 2011
Baseline acceptability of self vs. clinician testing

Mean total and sub-scale scores at baseline

Huppert et al. STI, 2011
Acceptability of self-testing increases with time

Mean sub-scale scores at each time point

Baseline | After testing | After discussion
---|---|---
Trust Result | | |
Confidence | | |
Comfort | | |
Self Efficacy | | |
Emergency Department Kiosk-facilitated POC TV Self-testing

Collecting the vaginal swab:

<table>
<thead>
<tr>
<th>Age</th>
<th>27.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>109</td>
</tr>
<tr>
<td>American</td>
<td>13</td>
</tr>
<tr>
<td>White</td>
<td>2</td>
</tr>
</tbody>
</table>

Prevalence 19.3%
# Results

## Patient acceptability before self-testing done

<table>
<thead>
<tr>
<th>Question</th>
<th>Will definitely be correct n (%)</th>
<th>Will probably be correct n (%)</th>
<th>Will not be correct n (%)</th>
<th>Missing n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you believe that the result of the Trichomonas Rapid Test will be correct, for the sample that you collect?</td>
<td>38 (30.6)</td>
<td>64 (51.6)</td>
<td>8 (6.5)</td>
<td>14 (11.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Very much n (%)</th>
<th>Somewhat n (%)</th>
<th>Not at all n (%)</th>
<th>Missing n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How much will you trust the result of the Trichomonas Rapid Test that you collect?</td>
<td>53 (42.7)</td>
<td>61 (49.2)</td>
<td>5 (4.0)</td>
<td>5 (4.0)</td>
</tr>
</tbody>
</table>
### Comparison of patient acceptability before and after self-test

<table>
<thead>
<tr>
<th>Question</th>
<th>Very hard n (%)</th>
<th>Somewhat hard n (%)</th>
<th>Not at all hard n (%)</th>
<th>Missing n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How hard will it be/was it for you to do the Trichomonas Rapid Test correctly?</td>
<td>6 (4.8)</td>
<td>35 (28.2)</td>
<td>78 (62.9)</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td></td>
<td>7 (5.6)</td>
<td>14 (11.3)</td>
<td>94 (75.8)</td>
<td>9 (7.3)</td>
</tr>
<tr>
<td><strong>After</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you think testing yourself is a good thing you can do for your health?</td>
<td>68 (54.8)</td>
<td>45 (36.3)</td>
<td>6 (4.8)</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td></td>
<td>89 (71.8)</td>
<td>25 (20.2)</td>
<td>1 (0.8)</td>
<td>9 (7.3)</td>
</tr>
<tr>
<td><strong>Before</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you think you will recommend to a friend that she test herself for Trichomonas?</td>
<td>85 (68.5)</td>
<td>24 (19.4)</td>
<td>8 (6.5)</td>
<td>7 (5.6)</td>
</tr>
<tr>
<td></td>
<td>96 (77.4)</td>
<td>15 (12.1)</td>
<td>4 (3.2)</td>
<td>9 (7.3)</td>
</tr>
<tr>
<td><strong>After</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Would you test yourself at home if the Trichomonas Rapid Test was available over-the-counter?</td>
<td>83 (66.9)</td>
<td>27 (21.8)</td>
<td>8 (6.5)</td>
<td>6 (4.8)</td>
</tr>
<tr>
<td></td>
<td>93 (75.0)</td>
<td>15 (12.1)</td>
<td>6 (4.8)</td>
<td>10 (8.1)</td>
</tr>
</tbody>
</table>
Results

READING ACCURACY:
Patient self-test interpretation vs coordinator interpretation

<table>
<thead>
<tr>
<th></th>
<th>TV positive n (%)</th>
<th>TV negative n (%)</th>
<th>Invalid n (%)</th>
<th>Missing n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Self-Test</td>
<td>23 (18.5)</td>
<td>90 (72.6)</td>
<td>2 (1.6)</td>
<td>9 (7.3)*</td>
</tr>
<tr>
<td>Coordinator Interpretation</td>
<td>24 (19.3)</td>
<td>88 (71.0)</td>
<td>3 (2.4)</td>
<td>9 (7.3)*</td>
</tr>
</tbody>
</table>

* 9 women did not complete self-testing

2 women incorrectly interpreted their self-test result:
  1 incorrectly labeled a positive result as negative (very faint test line)
  1 incorrectly labeled an invalid result as negative (no control line)
AmpliVue® Trichomonas Assay

1) simple sample preparation with one-step dilution/heating
2) isothermal DNA amplification of target sequences specific to *T. vaginalis* by HDA
3) lateral-flow strip based colorimetric detection in a self-contained, disposable device

Sensitivity 100%; specificity 98.2% vs. culture/wet prep. Vs. NAAT PPA 87.2-90.1%

Syphilis: Serologic DX requires detection of two types of antibodies

- Non-Treponemal  RPR, VDRL (Can be POC)
- Treponemal  FTA-abs, TPPA, Many new POC

- Biologic false positive non-treponemal test
- Falsely reactive treponemal test due to cross-reacting serum antibodies
- Both test types have imperfect specificity

- Reactive treponemal test cannot distinguish active from inactive infection
Syphilis serologic screening algorithms

**Traditional**

- Quantitative RPR
  - RPR+
    - TP-PA+ Syphilis (past or present)
  - RPR-
    - TP-PA- Syphilis unlikely
- RPR+
- TP-PA+ or other trep. test

**Reverse sequence**

- EIA or CIA
  - EIA/CIA+
  - EIA/CIA-
- Quantitative RPR
  - RPR+
    - Syphilis (past or present)
    - Evaluate clinically
  - RPR-
    - TP-PA
- TP-PA+ Syphilis (past or present)
- TP-PA- Syphilis unlikely

- CDC recommended algorithm for reverse sequence syphilis screening followed by nontreponemal test confirmation

- If at risk for syphilis, repeat RPR in several weeks

- Evaluate clinically
POC Syphilis Health Check™

Syphilis Antibody Rapid Immunochromatographic Test

• Rapid qualitative screening for human TP antibodies in whole blood, serum or plasma
• Results in 10 minutes; 2 steps; room temperature
• 98% agreement to other treponemal tests
• Serum, plasma or whole blood or finger-stick

Negative: 1 colored band in control area
Positive: Colored bands in test area and control area
Inconclusive: No distinct color bands in either area

FDA Cleared
CLIA Waived
Evaluation of an Immunochromatographic Point-of-Care Test for the Simultaneous Detection of Nontreponemal and Treponemal Antibodies in Patients With Syphilis

Rita Castro, MD, PhD,*† Ângela Lopes, Bsc,‡ and Filomena da Luz Martins Pereira, MD, PhD§

DPP Syphilis Screening & Confirm Assay (SSCA)

<table>
<thead>
<tr>
<th>SSCA</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compared to RPR</td>
<td>98.8%</td>
<td>94.7%</td>
</tr>
<tr>
<td></td>
<td>171/173</td>
<td>71/75</td>
</tr>
<tr>
<td>Compared to TPHA</td>
<td>95.5%</td>
<td>88.8%</td>
</tr>
<tr>
<td></td>
<td>184/185</td>
<td>56/63</td>
</tr>
<tr>
<td>Compared to FTA-abs</td>
<td>98.9%</td>
<td>93.2%</td>
</tr>
<tr>
<td></td>
<td>187/189</td>
<td>55/59</td>
</tr>
</tbody>
</table>

NOT Yet FDA Cleared
Sensitivity of Treponemal T1 compared to reference IA was 89.8% (95% CI, 87.3%–91.9%).

Specificity was 99.3% (95% CI, 97.0%–99.9%).

Sensitivity of Non-Treponemal T2 compared to reference RPR (reactive = RPR ≥1) was 94.2% (95% CI, 91.8%–96.0%).

Specificity 62.2% (95% CI, 57.5%–66.6%).
Distribution of rapid plasma reagin (RPR) titers among RPR (nontreponemal) reactive and immunoassay (treponemal) reactive reference test specimens (n = 525) and DPP T2 test line reactivity.

Determine™ Syphilis TP POC


**Dectes**
Antibodies to *Treponema pallidum* Recombinant TP (15kDa, 17kDa) antigens used as captures and detectors

**Rapid**
Provides accurate and reliable results in 15 minutes

**Convenient**
No refrigeration required (storage 2-30°C)
No power or water source is needed to run test

**Flexible**
Uses serum, plasma or whole blood by venipuncture or finger prick
What about Combination Syphilis and HIV POC tests?

These are coming soon—stay tuned

Here is a preview
• Chembio Diagnostic Systems has developed a dual HIV 1/2 and Syphilis Treponemal antibodies POC test (Dual Path Platform (DPP®) technology)

• Immunochromatographic rapid screening POC test

• Fingerstick whole blood, venous whole blood, serum, and plasma

http://www.youtube.com/watch?v=DE4Wxy4byQE&x-yt-ts=1401912551


3 minute test procedure
Whole blood, serum or plasma specimens
No specialized training required
Built-in procedural and reagent control line

18 month shelf-life at 2-30°C
No refrigeration or cold chain required
No timers required
Results are easy to interpret
No specialized equipment required
• SD BIOLINE HIV/Syphilis Duo test is a solid phase immunochromatographic assay
• Qualitative detection of antibodies to all isotypes (IgG, IgM, and IgA) specific to HIV-1/2 and/or *Treponema palladium* (TP)
• Serum, plasma, or whole blood

1-30°C for 24 months

http://www.standardia.com
2805 men with syphilis contributing 11,714 person-years of follow-up, 423 (15.1%) acquired HIV; annual incidence was 3.61% (95% CI, 3.27%, 3.97%).

HIV incidence was high among: MSM (5.56%, 95% CI, 5.02%–6.13%); males with secondary compared with primary syphilis (4.10% vs 2.64%, P < .0001); and males diagnosed with another bacterial STD after syphilis (7.89%, 95% CI, 6.62%–9.24%).

Hazard Ratio for MSM in multivariate analysis was 8.88
HIV

CLIA-Waived Point-of-Care Rapid HIV Tests

OraQuick Advance

Uni-Gold Recombigen

Alere

INSTI

Clearview Complete

Clearview Stat Pak
4th generation HIV-1/2 immunoassay

(-)

(+) Negative for HIV-1 and HIV-2 antibodies and p24 Ag

HIV-1/HIV-2 antibody differentiation immunoassay (i.e. Multispot rapid)

HIV-1 antibodies detected, Initiate care (and viral load)

HIV-2 antibodies detected, Initiate care

HIV antibodies detected

HIV-1 & 2 (-) or indeterminate RNA

RNA (+) Acute HIV-1 infection, Initiate care

RNA (-) Negative for HIV-1

HIV-1 +/HIV-2 + HIV antibodies detected

Good or Bad News to Test at Home?

Rapid HIV Testing at Home: Does It Solve a Problem or Create One?

Rochelle P. Walensky, MD, MPH, and A. David Paltiel, PhD

The U.S. Food and Drug Administration (FDA) is poised to approve over-the-counter rapid HIV tests. Home HIV testing will attract disproportionately of 'hard to reach' persons, as well as young "at risk" populations. Advocates of home testing claim that it will empower individuals to manage their HIV risks and increase rates of disease detection in communities that have proven difficult to reach and to link to appropriate care. The authors offer a more cautious perspective. According to what is already known about the market demand for over-the-counter HIV testing kits, their costs, and the performance of rapid HIV tests in that market, the authors do not anticipate that the rapid home test will have a profound impact either on the HIV public health crisis or on the curious population. Nevertheless, the authors illustrate how testing in these populations may have the perverse effect of increasing both false-negative and false-positive results. A poorly functioning home HIV test may thereby undermine confidence in the reliability of HIV testing more generally and weaken critical efforts to expand HIV detection and linkage to lifesaving care for the estimated 300,000 U.S. citizens with unidentified HIV infection.

For author affiliations, see end of text.
Among 827 sexually active non-HIV-positive participants, 89% had been tested for HIV. Most preferred by participants was home rapid testing (46%), followed by standard-of-care (23%) and rapid testing in healthcare (20%) or community settings (7%). About 73% of participants preferred rapid over non-rapid testing, and 56% preferred testing in non-healthcare settings rather than in healthcare settings.
Supervised and Unsupervised Self-Testing for HIV in High- and Low-Risk Populations: A Systematic Review


Stigma, discrimination, lack of privacy, and long waiting times partly explain why six out of ten individuals living with HIV do not access facility-based testing. By circumventing these barriers, self-testing offers potential for more people to know their sero-status. Recent approval of an in-home HIV self test in the US has sparked self-testing initiatives, yet data on acceptability, feasibility, and linkages to care are limited. We systematically reviewed evidence on supervised (self-testing and counselling aided by a health care professional) and unsupervised (performed by self-tester with access to phone/internet counselling) self-testing strategies.
Of the 21 studies included, 16 ($n = 16/21, 76\%$) were conducted in high-income versus five ($n = 5/21, 24\%$) in resource constrained country settings. Total sample size varied from 27 to 5,798. Two main strategies for HIV self-testing were identified, supervised and unsupervised, and the studies classification is illustrated in Figure 2.

The total sample size for the supervised testing strategy was 4,890 individuals and 7,512 for the unsupervised testing strategy. Our review provides data from 1,383 participants in resource constrained settings, compared to 11,019 in high-income settings, thus the bulk of data (89\%) was from high-income settings. Study populations varied from high at-risk for HIV to low-risk general populations.
Figure 2.

http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001414
Cost preference for self tests and willingness to pay if sold OTC were documented for both supervised and unsupervised strategies, and varied across populations, settings and strategies.

In supervised strategies, in Canada, 32% \( (n = 32/100) \) of university students were willing to pay up to US$10 and 41% \( (n = 41/100) \) up to US$20 while in Singapore, 88% \( (n = 370/420) \) were willing to pay between US$7 and US$13, and 28% \( (n = 118/420) \) more than US$15.

In a study in the US, 70% \( (n = 168/240) \) were willing to pay up to US$15, and 40% \( (n = 96/240) \) would be willing to pay US$20 for it. In another study in the US, at-risk participants from homeless shelters wanted free self tests.

In unsupervised strategies evaluated in an urban MSM population, 45% \( (n = 49/108) \) were willing to pay less than US$20, 25% \( (n = 27/108) \) between 20 and US$40, 17% \( (n = 18/108) \) more than US$40 and 13% \( (n = 14/108) \) wanted it free. Additionally, in Kenya, HCPs were unwilling to pay and wanted the government to provide it for free, as HIV was perceived to be an occupational risk. A study in Spain evaluating an unsupervised strategy in attendees at a rapid HIV testing site documented 18% \( (n = 56/313) \) willingness to pay more than US$38, 22% \( (n = 69/313) \) between US$25 and US$28 and 5% \( (n = 16/313) \) wanting it for free.
Instruction Guide

OraQuick HIV-1/2 Testing Instructions

OraQuick Kit:

1. Open first

A. OraQuick ADVANCE

B. Test Vial

C. Swab

2. Swab once around the gums, both top and bottom

3. Make sure that the swab rubs against the base of the gums

Insert device into Vial; then set timer for 20 minutes

NEGATIVE RESULT

Control Bar
Test Bar

POSITIVE RESULT

INVALID RESULT

C T
C T
C T
C T
C T
Emergency Departments: Critical Venue HIV Tests
Feasibility, Acceptability, and Accuracy,
Results

- Of 955 patients approached, 473 (49.5%) consented; 100% had concordant results with those obtained by health-care professionals.
- One new HIV infection identified in a 48 y woman.
- Median age was 41 years, 59.6% were female, 74.8% African American, 19.6% White.
- 99.8% of patients believed the POC self-test was “definitely” or “probably” correct, 91.7% of patients “trusted their results very much”.
- 99.8% reported that “overall” self-testing was “easy or somewhat easy” to perform.
**New Virus POC HSV Test- IsoAMP**

- FDA cleared POC assay for the detection of HSV in lesions; IsoAMP® HSV (Biohelix)
- Technology utilizes isothermal helicase dependent amplification (HAD), which uses Bst DNA polymerase, and by obviating the nucleic acid extraction process, with results in 1.5 hours
- From 5 sites in the U.S., after discordant analysis, overall agreement of IsoAmp with ELVIS was 98.8%, with a 37.0% overall prevalence
- Viral culture was used as the reference standard, the clinical sensitivity and specificity of the IsoAmp® HSV assay were 100.0% and 96.3% respectively. (5.5 and 34.1 copies/reaction for HSV-1-2)

---


The IsoAmp® HSV Assay (Biohelix Corp)

- FDA-cleared for HSV in genital and oral lesions
- The IsoAmp HSV has a test-to-result time of <1.5 hr.
- Isothermal helicase-dependent amplification (HDA) technique; no nucleic acid extraction
- The rapid and simple characteristics of the IsoAmp HSV assay make it potentially suitable for POC testing

Lemieux et al. Expert Reviews Ltd. 437-443, 2012;
Why do POCTs?

- Improve patient satisfaction (privacy)
- Treat patients before leave clinic
- Provide counseling on risk reduction
- Decrease interval of disease spread
- Improve clinical practice efficiency
- Improve medical outcomes

Published data to substantiate these claims are rare to date
Barriers to implementation of POCTs

- Financial viability
- Money for instruments and consumables
- Obtaining CLIA certificate
- Validating the new test(s)
- Policies and procedures (training manuals)
- Operator training (recertification, proficiency)
- Getting results into the EMR (interface- $7K?)
- Space
- Work Flow Disruption
- Billing and Reimbursement
Conclusions

• POCTs in primary/STI care have great potential

• But there are barriers to successful implementation that need to be overcome which can be costly, time consuming, and require learning new skill sets

• Better POC tests are coming; the future is promising
Outside the Clinic: IWTK Methods

- 2004-13: Orders a kit on line & select Rx clinic
- Kit mailed to home
- Collect sample at home
- Mail kit to lab
- Text or Email sent for when results are ready
- 2013-15 Revised
- Patient has password protected account and obtains results on line and attends clinic of choice to receive treatment
- Attends a clinic for Rx

www.iwantthekit.org
<table>
<thead>
<tr>
<th>Gender</th>
<th>Location</th>
<th>Sample Size</th>
<th>Year</th>
<th>CT: Prevalence</th>
<th>GC: Prevalence</th>
<th>TV: Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEMALE</td>
<td>Vaginal</td>
<td>6207</td>
<td>2004</td>
<td>7.2%</td>
<td>0.8%</td>
<td>6.9%</td>
</tr>
<tr>
<td>MALE</td>
<td>Penile</td>
<td>3279</td>
<td>2006</td>
<td>8.2%</td>
<td>0.8%</td>
<td>2.6%</td>
</tr>
<tr>
<td>FEMALE</td>
<td>Rectal</td>
<td>1055</td>
<td>2009</td>
<td>7.4%</td>
<td>1.0%</td>
<td>6.5%</td>
</tr>
<tr>
<td>MALE</td>
<td>Rectal</td>
<td>632</td>
<td>2009</td>
<td>7.8%</td>
<td>4.6%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>
STI Prevalence of 3363 Female Internet STD Screening Program Participants by Calendar Year

Prevalence (%)

- Chlamydia
- Gonorrhea
- Trichomonas


Sample Size:
- 2004: n=380
- 2005: n=190
- 2006: n=189
- 2007: n=306
- 2008: n=444
- 2009: n=701
- 2010: n=374
- 2011: n=779
# Yearly Internet Tests

## Kits requested:

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaginal</th>
<th>Female Rectal</th>
<th>Penile</th>
<th>Male Rectal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>749</td>
<td>155</td>
<td>421</td>
<td>103</td>
<td>1515</td>
</tr>
<tr>
<td>2012</td>
<td>961</td>
<td>221</td>
<td>572</td>
<td>99</td>
<td>1853</td>
</tr>
<tr>
<td>2013</td>
<td>907</td>
<td>221</td>
<td>688</td>
<td>148</td>
<td>1964</td>
</tr>
<tr>
<td>2014</td>
<td>821</td>
<td>214</td>
<td>556</td>
<td>182</td>
<td>1773</td>
</tr>
</tbody>
</table>

2012: 3,599  
2013: 3,035

Return rate: 2004-7 ~30%; 2011: 42.4%; 2012: 51.5%; 2013: 64.7%; 2014: 65.1%

Postage ($2.40) required for return kits as of July 2014
Self-Collection of Vaginal Swab

ATTENTION: Read ALL instructions before you begin!

**STEP 1**
Wash your hands thoroughly.

**STEP 2**
Undress from the waist down. Get into a position where you can comfortably insert a swab into your vagina—such as sitting on the toilet, or standing with one foot on a chair, or any position that you would use to insert a tampon.

**STEP 3**
Take the sealed swab out of the package. Open the swab.
Twist first to break seal.
Then pull. The swab will stay attached to the red cap.
Do NOT throw the plastic tube away! You will need to put your swab in it after you have collected the sample.

**STEP 4**
Insert the white tip of the swab about one inch inside the opening of your vagina.

**STEP 5**
Rotate the swab for 15 seconds, making sure that the swab touches the walls of your vagina so that moisture is absorbed into the swab.

**STEP 6**
Remove the swab from your vagina. Don't let the tip of the swab touch anything else.

**STEP 7**
Place used swab back into the transport tube. Close tightly to prevent leakage.

**STEP 8**
Place closed tube into the red plastic zip-lock bag. Seal the bag.

**STEP 9**
Place sealed zip-lock bag into the return mailer (yellow envelope). Seal the envelope and drop it in any mailbox. It’s already addressed and postage is paid, so you don't need to do anything else.

Peel off adhesive to reveal seal.
Self-Collection of Penile Swab
ATTENTION: Read ALL instructions before you begin!

STEP 1
Take the sealed swab out of the package. Open the swab.

Twist first to break seal.

Then pull. The swab will stay attached to the red cap.

Do NOT throw the plastic tube away! You will need to put your swab in it after you have collected the sample.

STEP 2
Roll the swab just at the tip or inside the opening to the penis through which you pass urine (pee). Roll the swab completely around the opening to get the best specimen. It is not necessary to put the swab deep inside the hole (urethra opening).

Roll the swab around the edges of the urethra opening. (The swab can touch the edges of the hole, but don’t push it inside.)

STEP 7
Place used swab back into the transport tube. Close tightly to prevent leakage.

STEP 8
Place closed tube into the red plastic zip-lock bag. Seal the bag.

STEP 9
Place sealed zip-lock bag into the return mailer (yellow envelope). Seal the envelope and drop it in any mailbox. It’s already addressed and postage is paid, so you don’t need to do anything else.
Male Questionnaire Results
Home collection (N = 501) Chai et al.

- **Penile Swab**
  - Collection Easy to Very Easy: 89.8%
  - Instructions Easy to Very Easy: 94.0%
  - Use Internet-based SAS again: 91.4%

- **Urine**
  - 95.3%

No swab: 8; No urine 2
Self-Collection of Rectal Swab
ATTENTION: Read ALL instructions before you begin!

STEP 1
Wash your hands thoroughly.

STEP 2
Unopened Swab
Either squat down, or lift one leg on a toilet, ledge, or chair (as shown). Pull underwear down or off.

STEP 3
Open the swab.
DO NOT TOUCH THE TIP OF THE SWAB.
 Twist first to break seal.
Then pull. The swab will stay attached to the red cap.
Do NOT throw the plastic tube away! You will need to put your swab in it after you have collected the sample.

STEP 4
With your dominant hand (right if you're right-handed, left if you're left-handed), grip the opened swab 1.5" away from the tip of the swab (just below the first notch). DO NOT TOUCH THE TIP OF THE SWAB.

Do NOT, at any point, use anything (soap, saliva, or any kind of lubricant) either on your body or on the swab.

STEP 5
With your other hand, position your bare buttock and lift one cheek for easy access to the rectum. (DO NOT use anything on your rectum or the swab.)

STEP 6
Insert the swab 1.5 inches into your rectum until you feel your fingers touch your anus.

STEP 7
Once the swab is in, walk your fingers halfway down the swab (away from your body) and grip it there, for stability. (The swab should stay where it is—only your fingers should move.)

STEP 8
Gently rub the swab in a circle, touching the walls of your rectum, to collect the specimen.

STEP 9
When removing the swab from your rectum, slowly turn it into a circle while pulling it out.

STEP 10
Place used swab back into the transport tube. Close tightly to prevent leakage.

STEP 11
Place closed tube into the red plastic zip-lock bag. Seal the bag.

STEP 12
Place sealed zip-lock bag into the return mailer (yellow envelope). Seal the envelope and drop it in any mailbox. It’s already addressed and postage is paid, so you don’t need to do anything else.
Proportion of Infections Detected by Rectal or Genital Sampling

Van Der Pol, BASHH 2012

<table>
<thead>
<tr>
<th></th>
<th>CT Male</th>
<th>GC Male</th>
<th>CT Female</th>
<th>GC Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Only</td>
<td>9</td>
<td>55</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Both</td>
<td>24</td>
<td>14</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>Genital only</td>
<td>80</td>
<td>55</td>
<td>17</td>
<td>10</td>
</tr>
</tbody>
</table>
The revised Web site implemented an automated test result access system. To evaluate potential deleterious effects of the new system, we analyzed demographics, Web site usage, and treatment. The post–Web site design captured more participant information and no decrease in requests, kit return, or treatment adherence.
## IWTK Risk Score

<table>
<thead>
<tr>
<th>Questions</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are you ≤ 25 years old?</td>
<td>Yes = 1 point.  No = 0 points.</td>
</tr>
<tr>
<td>2. Have you had a new sex partner, or multiple partners, in the last 90 days?</td>
<td>Yes = 1 point.  No = 0 points.</td>
</tr>
<tr>
<td>3. Do you have more than one current sex partner at the present time?</td>
<td>Yes = 1 point.  No = 0 points.</td>
</tr>
<tr>
<td>4. Have you ever been told you had, or been treated for, and STI in the past?</td>
<td>Yes = 1 point.  No = 0 points.</td>
</tr>
<tr>
<td>5. How many sex partners have you had in the last 90 days?</td>
<td>10 or more = 3 points.  5-9 = 2 points.  2-4 = 1 point.  0-1 = 0 points.</td>
</tr>
<tr>
<td>6. When you have sex, do you use a condom?</td>
<td>Never = 3 points.  Sometimes = 3 points.  Always = 0 points.</td>
</tr>
</tbody>
</table>
Prevalence of Sexually Transmitted Infections (Chlamydia, Gonorrhoea, and Trichomonas) by Gender and I Want the Kit (IWTK) Risk Score (N=1,394)
Multivariate Logistic Regression Analysis on the Association of I Want the Kit (IWTK) Risk Score and Prevalence of Sexually Transmitted Infections (Chlamydia, Gonorrhea, and Trichomonas) by Gender

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Categories</th>
<th>Female</th>
<th>Male†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>&lt; 20</td>
<td>3.15 (1.58, 6.30)</td>
<td>N.S.</td>
</tr>
<tr>
<td></td>
<td>20 – 29</td>
<td>1.56 (0.92, 2.66)</td>
<td>N.S.</td>
</tr>
<tr>
<td></td>
<td>≥ 30</td>
<td>1.00</td>
<td>N.S.</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>2.63 (1.52, 4.58)</td>
<td>5.69 (1.96, 16.59)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2.92 (1.52, 5.62)</td>
<td>4.01 (1.09, 14.68)</td>
</tr>
<tr>
<td>Risk Score Category*</td>
<td>“Low Risk”</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>“Medium Risk”</td>
<td>2.23 (1.41, 3.52)</td>
<td>1.84 (0.42, 8.11)</td>
</tr>
<tr>
<td></td>
<td>“High Risk”</td>
<td>4.22 (2.08, 8.58)</td>
<td>3.88 (0.85, 17.69)</td>
</tr>
</tbody>
</table>

Risk Score Category: defined by prevalence of STIs for each gender. **Females:** Risk score of 0-4 was categorized as “low risk”, risk score of 5-7 as “medium risk”, and risk score of 8-10 as “high risk”; **Males:** risk score of 0-2 was categorized as “low risk”, risk score of 3-6 as “medium risk”, and risk score of 7-10 as “high risk”
Trichomonas IWTK Home Test

**IWTK is recruiting for a Trich study. Would like you to participate?**

![Johns Hopkins Medicine Logo](image)

**Why is this research being done?**

*Trichomonas vaginalis* is a common sexually transmitted infection of the genital tract that can infect both men and women. Rapid diagnosis and correct treatment are very important in the management of genital tract infections and help to prevent serious complications.

This research is being done to evaluate the acceptability and accuracy of performing an investigational, single-use, rapid point-of-care test for *Trichomonas vaginalis* at home by participants from the ‘I Want the Kit’ (IWTK) project.

The word “investigational” means the single-use Trichomonas Rapid Test is not approved by the U. S. Food and Drug Administration (FDA) and is still being tested in research studies.

We will ask you to run the investigational, single-use Trichomonas Rapid Test (which is similar to the OSOM® Trichomonas Rapid Test which is FDA-approved and CLIA-waived).

We want to find out if the test is easy to perform, and to compare the results that you get at home with the results that the laboratory gets from the swab that you collect and mail back for testing.

**What will happen if you join this study?**

If you agree to be in this study, we will send you a single-use Trichomonas Rapid Test with your IWTK Vaginal Kit and ask you to do the following things:
## Trichomoniasis Home Test Analysis

<table>
<thead>
<tr>
<th>Question, N = 92</th>
<th>Easy</th>
<th>Somewhat Easy</th>
<th>Not Easy</th>
</tr>
</thead>
<tbody>
<tr>
<td>How easy was it for you to collect the vaginal specimen correctly?</td>
<td>88 (95.6%)</td>
<td>3 (3.3%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>How easy was it for you to read the test strip and interpret (tell) the result?</td>
<td>84 (91.3%)</td>
<td>6 (6.5%)</td>
<td>2 (2.2%)</td>
</tr>
<tr>
<td>Overall, how easy was it for you to perform the test?</td>
<td>85 (92.4%)</td>
<td>5 (5.4%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Do you believe that the rapid trichomoniasis test result was correct for the sample that you collected?</td>
<td>52 (56.5%)</td>
<td>39 (42.4%)</td>
<td>1 (1.1%)</td>
</tr>
</tbody>
</table>
## Trichomonas Home Test Analysis

<table>
<thead>
<tr>
<th>Question</th>
<th>Trust very much</th>
<th>Trust Somewhat</th>
<th>Do Not Trust</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How much do you trust the result of the rapid trichomonas test</strong></td>
<td>60 (65.2%)</td>
<td>31 (33.7%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>that you collected and tested?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Definitely Test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Would you test yourself at home for trichomonas</strong></td>
<td>77 (83.7%)</td>
<td>14 (15.2%)</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td><strong>if the rapid trichomonas test were available over-the-counter?</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Not Test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>What is the maximum price you would pay to purchase a rapid</strong></td>
<td>42 (45.6%)</td>
<td>37 (40.2%)</td>
<td>3 (14.1%)</td>
</tr>
<tr>
<td><strong>trichomonas test over-the-counter, if available?</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>$10</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>$20</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>$30</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
- Based on your experience, would you prefer to test yourself for trichomonas at home or would you prefer a healthcare provider/laboratory collect and perform your test?

1. Prefer self-testing 54 (58.7%)
2. Prefer healthcare provider/laboratory 8 (8.7%)
3. No Preference 29 (31.5%)
   No Response 1 (1.1%)

- If you went to a clinic, doctor’s office, or emergency room to see a healthcare provider, which would you prefer?

1. To have the healthcare provider collect your sample and perform the test 33 (35.9%)
2. To collect the sample yourself and have the healthcare provider perform the test 30 (32.6%)
3. To collect the sample yourself and perform the test yourself in the clinic/doctor’s office/ER 2 (2.2%)
4. No Preference 27 (29.3%)
### Trichomonas Home Test Analysis

<table>
<thead>
<tr>
<th>Interpretation of self-test result by participant</th>
<th>GenProbe SOC TV results</th>
<th>SOC swab not returned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive 1* (* vaginal &amp; rectal TV+ by SOC)</td>
<td>0</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>82§ ($3 of 82 CT+ by SOC)</td>
</tr>
<tr>
<td>Invalid</td>
<td>0</td>
<td>2€ ($1 of 2 rectal TV+ by SOC)</td>
</tr>
<tr>
<td>“Don’t Know”</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

There were 4 participants who returned their SOC swab for testing but did not enter their results/interpretation for their self-test or take the survey:
2 = SOC negative. 1 = SOC TV+. 1 = SOC CT+. 

N = 86
IWTK TV POC Conclusions

• Moderate to high patient acceptability

• Loss of patients due to multiple website contacts needed

• Patients can reliably collect, perform and read POC test with kit and web-based instructions

• Low positivity –”Worried Well”
Results: The internet-based screening strategy prevented 35.5 more cases of pelvic inflammatory disease and saved an additional $41,000 in direct medical costs as compared with the clinic-based screening strategy.

Conclusion: Our model estimates demonstrated that an internet based, self-swab screening strategy was cost-effective compared with the traditional, clinic-based screening strategy.

Assuming that the popularity of the use of the internet as a resource for information about healthcare and sexually transmitted infections leads to an increased use of IWTK, the public health benefit of this cost-effective strategy will be even greater.
Results indicate that eSTI will likely be more cost-effective (lower cost/STI detected) than clinic-based STI screening, both in the context of clinical trials and in routine clinical care. Although our results are promising, they are based on a demonstration project and estimates from other small studies.

A comparative effectiveness research trial is needed to determine actual cost and impact of the eSTI system on identification and treatment of new infections and prevention of their sequelae.
We are trying to POINT the WAY for POC Tests

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• Jeff Holden
• Laura Dize
• Perry Barnes
• Billie Masek
• Brianna Kyburz

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POCT – Build Your Own Test

• First Priority of Needs Assessment Survey
  – Chlamydia (62%); HIV – Early Seroconversion (14%)
  – Syphilis (8%)

• Overall, participants selected sensitivity as their top priority, followed by cost, specificity, and time

• Choices (statistically significant)
  Sensitivity: 90-99% > 80-90% > 70-80%
  Cost: $20 > $ 35 > $50
  Specificity: 99% > 95% > 90%
  Time: 5 > 15 > 25 minutes

Key Applications

Sexually Transmitted Infections

Focusing on key applications where a rapid, actionable test result can improve patient outcomes

- Immediate treatment of positive patients
- Expedite appropriate therapy
- Reduce empirical treatment
- Lower risk of antibiotic resistance
- Improve compliance / minimize loss to follow-up
- Reduction in patient pathway costs
- Decrease forward transmission
- Lower risk of sequelae
- Improve the patient experience
Technology

Electrochemical detection – facilitates fast, low cost diagnostics

- Proprietary detection technology
- Sensitive
- Wide dynamic range
- High multiplex capability by use of different ferrocene derivatives
- No need for optical sensors. Robust, no calibration
- Quantitative
- No restrictions on Cartridge materials. Optical clarity not needed.
Why is the impact of TV important?

Trichomonas and HIV acquisition

Laga 1993 OR 1.9 (0.9-4.1)
Laga 1994 RR 1.7 (1.1-2.8)
Taha RR 1.88 (1.32-3.38)
Ghys RR 2.4 (1.1-5.2)
Myer RR 1.84 (1.02-3.32)
Kleinschmidt HR 4.8 (1.0 to 22.8)
McClelland RR 1.52 (1.04-2.24)
Van Der Pol OR 2.74 (1.25 to 6.00)
Mavedzenge HR 2.05 (1.05 to 4.02)
Delany-Moretlwe RR 2.3 (1.1-4.9)
Vandepitte HR 2.72 (1.27 to 5.84)
Quinn RR 1.84 (0.84-3.89)
Hester OR 2.77 (0.83-9.19)
Hughes RR 2.57 (1.43 to 4.65)
<table>
<thead>
<tr>
<th>Organism</th>
<th>Test</th>
<th>Sample Type</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV*</td>
<td>OraQuick Advance Rapid HIV-1/2 Antibody Test</td>
<td>Oral Fluid, Whole blood/Serum</td>
<td>99.6%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Reveal G3 Rapid HIV-1 Antibody Test</td>
<td>Serum/Plasma</td>
<td>99.8%</td>
<td>99.9%</td>
</tr>
<tr>
<td></td>
<td>Multispot HIV-1/HIV-2 Rapid Test</td>
<td>Serum/Plasma</td>
<td>100%</td>
<td>99.9%</td>
</tr>
<tr>
<td></td>
<td>Uni-Gold Recombigen HIV Test</td>
<td>Whole blood/Serum/Plasma</td>
<td>100%</td>
<td>99.7%</td>
</tr>
<tr>
<td></td>
<td>Clearview HIV-1/2 Stat-Pak or Clearview Complete HIV ½</td>
<td>Whole blood/Serum/Plasma</td>
<td>99.7%</td>
<td>99.9%</td>
</tr>
<tr>
<td></td>
<td>Chembio DPP HIV1/2 Assay</td>
<td>Oral Fluid, Whole blood/Serum/Plasma</td>
<td>99.8%</td>
<td>99.9%</td>
</tr>
<tr>
<td></td>
<td>INSTI HIV-1 Antibody Test</td>
<td>Whole blood/Plasma</td>
<td>99.8%</td>
<td>99.5%</td>
</tr>
</tbody>
</table>


*Adapted and Updated from Huppert et. al. (2010) and Branson (2007)
<table>
<thead>
<tr>
<th>Organism</th>
<th>Test</th>
<th>Sample Type</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>Biostar OIA Chlamydia test</td>
<td>Cervical</td>
<td>59.4-73.8%</td>
<td>98.4-100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male Urine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clearview Chlamydia</td>
<td></td>
<td>Cervical</td>
<td>49.7%</td>
<td>97.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginal</td>
<td>32.8%</td>
<td>99.2%</td>
</tr>
<tr>
<td>Quick Vue</td>
<td></td>
<td>Cervical</td>
<td>25-65%</td>
<td>100%</td>
</tr>
<tr>
<td>Chlamydia Rapid Test</td>
<td></td>
<td>Vaginal</td>
<td>83.5%</td>
<td>98.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male Urine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-pert CT/NG</td>
<td></td>
<td>Cervical</td>
<td>97.4%</td>
<td>99.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginal</td>
<td>98.7%</td>
<td>99.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female Urine</td>
<td>97.6%</td>
<td>99.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male Urine</td>
<td>97.8%</td>
<td>99.9%</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>Biostar OIA GC test</td>
<td>Cervical</td>
<td>60%</td>
<td>89.9%</td>
</tr>
<tr>
<td>PATH GC-Check</td>
<td></td>
<td>Cervical</td>
<td>70%</td>
<td>97.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginal</td>
<td>54.1%</td>
<td>98.25</td>
</tr>
<tr>
<td>X-pert CT/NG</td>
<td></td>
<td>Cervical</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginal</td>
<td>100%</td>
<td>99.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female Urine</td>
<td>95.6%</td>
<td>99.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male Urine</td>
<td>98.9%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

Adapted from Huppert et al. (2010). * Sensitivity and specificity compared to NAATs
DPP HIV-1/2 Assay: Now CLIA Waived

• Moderate complexity for serum, plasma, oral fluid
• “Sample Tainer” = residual specimen after testing
• FDA-approved Dec 21, 2012
• CLIA for Fingerstick or Oral fluid
New CDC Recommendations for HIV Testing in Laboratories

A step-by-step account of the approach

CDC's new recommendations for HIV testing in laboratories capitalize on the latest available technologies to help diagnose HIV infections earlier – as much as 3-4 weeks sooner than the previous testing approach. Early diagnosis is critical since many new infections are transmitted by people in the earliest (“acute”) stage of infection.

By putting the latest testing technology to work in laboratories across the United States, we can help address a critical gap in the nation’s HIV prevention efforts.

Step 1: “Fourth generation” HIV test
Detecting HIV sooner

Step 2: HIV-1/HIV-2 antibody differentiation immunoassay
Diagnosing HIV-1 vs. HIV-2

- Produces results faster than the previously recommended Western Blot.
- Distinguishes between HIV-1 and HIV-2, which the previously recommended Western Blot cannot do – this distinction can have important treatment implications for a patient.

Step 3: Nucleic Acid Test (NAT)
Acute HIV-1 infection or “false positive”?

- Ensures accurate detection of early infection or indicates a false positive from the fourth generation test.

This graphic is designed to illustrate key concepts of the new testing approach in laboratories. For more detail, please see the full guidelines here:

www.cdc.gov/nchhstp/newsroom
What qualities do providers identify as best for POC STI tests: Do opinions differ by practice, region and country?

Results:

• 190 subjects replied to the survey: 46% male and 54% female

• Europe (27%), Oceana (26%), America (22%), Africa (11%), Asia (11%)

• The majority (61%) were from developed countries

• **Unreliability** (19.5%) was the characteristic considered the greatest barrier for use of POCTs, followed by a technology that was laboratory-driven (12%) and complexity (12%) of performing the test.
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001414
# Sensitivities and Specificities for Serology & POC Diagnostics for HSV-2

<table>
<thead>
<tr>
<th>Herpes Simplex Virus 2 (HSV-2)</th>
<th>Test</th>
<th>Sample Type</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serology</td>
<td>HerpeSelect</td>
<td>Serum</td>
<td>80-100%*</td>
<td>41-100%*</td>
</tr>
<tr>
<td></td>
<td>HerpeSelect</td>
<td>Serum</td>
<td>91%**</td>
<td>97%**</td>
</tr>
<tr>
<td>Serology</td>
<td>Kalon HSV-2 gG2</td>
<td>Serum</td>
<td>84-98.6%*</td>
<td>83.2-100%*</td>
</tr>
<tr>
<td>Virus</td>
<td>Rapid Real-Time PCR LDT ABI7500 Fast</td>
<td>Genital lesions</td>
<td>96.7%***</td>
<td>99.6%***</td>
</tr>
<tr>
<td>Virus</td>
<td>Qx PCR (BD)</td>
<td>Lesion vs. PIS</td>
<td>95.9-97.3%*</td>
<td>95.7-100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lesion vs. PCR</td>
<td>95.7-100%</td>
<td>95.8-100%</td>
</tr>
<tr>
<td>Virus</td>
<td>IsoAMP HSV POC (Biohelix)</td>
<td>Genital swabs</td>
<td>97.1%****</td>
<td>93.4%****</td>
</tr>
</tbody>
</table>


Adapted from Biaro et al. (2011). Sensitivity and specificity are expressed as a range from multiple studies over multiple years from the meta-analysis. **Adapted from Zahariadis et. al. (2010); ***Adapted from Gardella et. al. (2010); †Van Der Pol et al. J Clin Microbiol 2012;51:3466-3471. ****Adapted from Lemieux et. al. (2012)
The World

North America: 22%
Europe: 27%
Asia: 11%
Africa: 11%
South America: 11%
Oceania: 26%

© MapQuest
Profession (N =190)

- MD: 63%
- Non-MD professional: 15%
- Academic: 7%
- Health Worker: 4%
- Lab Professional: 11%
- Other: 4%
<table>
<thead>
<tr>
<th>Condition</th>
<th>% Respondents from Developed Country</th>
<th>% Respondents from Resource Constrained Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>56</td>
<td>26</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Hepatitis B/C</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Herpes Simplex Virus</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>HIV (early Seroconversion)</td>
<td>21</td>
<td>31</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Syphilis</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
The greatest barrier for use of POCTs (n=190)

- Unreliability: 19%
- Laboratory-driven: 12%
- Complexity: 12%
- Time Frame: 12%
- Patient wait time: 12%
- workflow interruption: 10%
- other: 7%
- 24%

(no differences between developing and developed for the top 3)
Important Drivers of POC Adoption

- Sensitivity, specificity, and time are important
- Willingness to pay the cost is important
- Willingness to self-collect specimens is probably important
- What about the patient’s needs?
TV ED Conclusions

• Baseline moderate to high patient acceptability – improved with real-life experience

• Clinicians indicated POC test impacted management in nearly 50% of cases

• Patients reliably collect, perform and read POC test with kiosk instructions

• POC test increased rates of detection of infection